UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DATE: July 27, 2000

MEMORANDUM

SUBJECT: Diclofop-methyl (PC Code 110902): HED's Response to Comments Submitted During 30-Day Registrant Error Correction Period. DP Barcode D267139.

FROM: Christina Jarvis, Risk Assessor
Reregistration Branch II
Health Effects Division (7509C)

THROUGH: Alan Nielsen, Branch Senior Scientist
Reregistration Branch II
Health Effects Division (7509C)

TO: Anne Overstreet, Chemical Review Manager
Reregistration Branch III
Special Review and Reregistration Division (7508W)

INTRODUCTION:

The Health Effects Division (HED) acknowledges the comments received from Aventis Crop Science during the 30-day registrant error correction period for diclofop-methyl (J. Barron letter, 6/30/2000). Attached are HED's responses to the comments submitted by Aventis. Where applicable, Aventis' comments have been incorporated into HED's revised disciplinary chapters. Input has been provided by Robert Fricke (toxicology), Rich Griffin (dietary exposure), Sheila Piper (residue chemistry), and Seyed Tadayon (occupational exposure).

I. TOXICOLOGY:

Aventis' Comment:

Aventis does not agree with the EPA's conclusion that a linear low-dose approach (Q*) should be used for the assessment of chronic cancer risk for diclofop-methyl, based on mouse liver tumors.

HED's Response:

On March 27, 2000, the Health Effects Division's Mechanism of Toxicity Assessment Review Committee (MTARC) and Cancer Peer Review Committee met to discuss mode of action on liver carcinogenicity of diclofop-methyl. The Committees felt that:

a.) Although hepatomegaly, as measured by increased relative liver weight, was a consistent finding in both rats and mice, no evidence was presented on actual measurement of the number of peroxisomes using morphometric analysis.

b.) Increased catalase activities were used as evidence of peroxisome proliferation. The committee felt that measurement of acyl or palmitoyl CoA oxidase activities would be more sensitive indicators of peroxisome proliferation.

c.) Electron micrographic evidence for peroxisome proliferation was very limited and consisted of evaluation of high-dose animals (one/sex) from a mouse oncogenicity study and a 90-day feeding study in the rat. Control or intermediate dose animals were not examined, which makes evaluation of possible dose-response relationships impossible to determined.

d.) The data for diclofop-methyl are not at par with that of fomesafen, which included measurement of hepatic palmitoyl CoA oxidase activities and determination of peroxisome volume using morphometric analysis.

Aventis' Comment:

A NOAEL based on a chronic feeding/carcinogenicity study in rats is inappropriate to assess single exposures or intermittent exposures of less than one week to several months, when toxicity studies of more relevant dosing duration are available. The 90-day feeding study in rats is more appropriate for the short-term inhalation risk assessment endpoint than the chronic feeding/carcinogenicity study in rats.

HED's Response:

The HIARC concurred with the Registrants proposed study to be used for acute and intermediate-term inhalation exposure. These endpoints will be established using NOAEL of 1.6

mg/kg/day from a subchronic feeding study in the rat (425733010).

II. DIETARY RISK ASSESSMENT:

Aventis' Comment:

Aventis found numerous calculation, round-off, and data transcription errors in the EPA document. A full description of the method used to calculate tissue to feed transfer factors could not be found. Aventis was unable to validate EPA dietary burden calculations from the residue data and dietary contributions presented in the EPA document. Aventis has recalculated the animal diet, residue transfer factors, and the anticipated meat and milk residues. The EPA chronic residue value of 0.0004 ppm is incorrect; the correct residue value should be 0.0003 ppm or less because the average percent crop treated for barley is 3%. The residue value for whole milk should be applied to all four milk fractions, rather than the residue value for skim milk.

HED's Response:

The Agency acknowledges Aventis' comments regarding the dietary risk assessment. Based on comments made by the registrant, and based on further analysis of current use practices of diclofop-methyl on wheat forage for dairy cattle, the dietary exposure assessment has been refined.

III. NON-DIETARY EXPOSURE ASSESSMENT

Aventis' Comment:

The default turf transferable residue (TTR) value of 5% of the application rate that was used in the Agency's risk assessment can be replaced with a TTR value of 0.30% of the application rate (Day 0) from ORETF data. The use of ORETF data in place of the default assumptions used by the Agency will refine the golfer cancer risk to a level that is traditionally acceptable to the Agency.

HED's Response:

The HED Residential Exposure SOPs currently estimate the Turf Transferrable Residue (TTR) to be 5 % of application rate on the day of application. In the case of diclofop-methyl, the risks at day zero using current defaults is acceptable. Data obtained from the Outdoor Residential Exposure Task Force (ORETF) needs to be reviewed and finalized by HED. Once this is accomplished, the ORETF data will replace the current default value. Finally, ORETF has not addressed golfer exposure in any dermal exposure study.

Aventis' Comment:

The use of 350 acres treated per day for aerial applications to wheat and barley will overestimate the expected area treated because of the limited use of diclofop-methyl. The 350 acres treated per day aerial default value should be refined to 75 acres treated per day, based on California records of aerial application.

HED's Response:

Current HED policy (revised July 05, 2000) provides standard values for the number of acres that can be treated in a single day by a fixed-wing aircraft. Values used for aerial application of barley and wheat are currently 350-1200 acres for commercial applicators (these values used in assessment for entire United States). The acreage used for aerial application is based on the following data:

National Agricultural Aviation Association's 1998 Industrial Survey for Agricultural Aviation (values for acres treated per day range from 1,017 to 1,643 acres for all crops, and 970 to 1,625 acres for wheat); N. Akesson and W. Yates. 1974.

Food and Agriculture Organization of the United Nations Agricultural Development Paper No. 94, titled "The Use of Aircraft in Agriculture."

PHED application data normalized to an 8 hour day (1,380 acres treated per day, average) and cultural use patterns.

The aerial application for diclofop-methyl was assessed at 350 acres per day, which is the low end of the range of current policy. Considering the above data from valid sources, the use of 350 acres per day for aerial application of diclofop-methyl is justified at the current time.